Application No. 10/790,338

REMARKS

Claims 54-104 and 151-209 are pending. By this Amendment, claims 198, 207, and 208 are cancelled without prejudice. New claims 210 and 212 are directed to a coating only on a solid portion of the stent, e.g., as at page 18, lines 4-16. New claims 211 and 213 are directed to a coating applied on both a lumen and an exterior of a stent, e.g., as at page 18, line 1. New claims 214 and 215 specify a particular glass transition temperature, e.g., as at page 6, line 2. Claims 54, 151, and 190 are amended to specify an uncrosslinked copolymer, e.g., as at Examples 1-8 wherein no crosslinker was used to prepare or use the copolymer or coating. Claim 82 was amended for antecedent basis. Claims 97-99 and 170 are amended to specify the claimed glass transition temperature for the coating, e.g., as at page 12, lines 5-19 of the Application, and to clarify that differential scanning calorimetery relates to a measurement process, not a calculation process. Claim 151 is further amended to recite a coating, e.g., as at page 4, lines 4-14, and to delete "a composition associated with at least a portion of every". Claims 167, 170, and 206 are amended to delete the word "about". Claim 169 is amended for antecedent basis. Claim 190 is amended to delete "expandable stent".

The specification is amended as indicated to remove a formula for glass transition temperatures and a calculation thereof. This amendment does not raise 35 U.S.C. §112 issues since the deleted formula does not implicate the claimed glass transition temperatures taken by differential scanning calorimetery and because other formulas for calculating the same values are known to those skilled in the art, e.g., as in the Alvarado reference discussed below, and as described in the previous amendment.

I. Claims 167, 170-189, 206, and new claims 214-215.

Claims 167, 170-182, and 206 stand rejected under 35 U.S.C. §103(a) in light of U.S. Pat. No. 6,530,950 (Alvarado et al.) in combination with U.S. Pat. No. 5,637,113 (Tartaglia). Claims

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183-185 stand rejected under 35 U.S.C. §103(a) in light of Alvarado et al. in combination with Tartaglia and U.S. Pub. 2002/0133183 (Lentz). Amended claims 167, 170-189, and 206 are directed to a copolymer or coating with a glass transition temperature between 26 and about 40 degrees Centigrade. New claims 214 and 215 are directed to a glass transition temperature of about 37°C. In contrast, Alvarado teaches that an "the polymers of the inventions, as exemplified by those described in Tables 1-6, have glass transition temperatures *below* 25°C.

The Office Action has rejected the indicated claims on the grounds that "about 26°C" reads on Alvarado. The amended claims delete the word "about" such that the claims are understood to be free of the prior art.

Claims 67, 170-189, and 206 have also been rejected under 35 U.S.C. §112¶1 for lack of support for the limitation "about 26°C". The Application discloses, at page 6, lines 1-2 "an average Tg that approaches a physiological temperature of about 37° C". It is submitted that 26° C is understood by ordinary artisans as approaching a physiological temperature. As discussed above, the Application further discloses the role of Tg with respect to release of a therapeutic agent, so this portion of the disclosure can reasonably be read with a wide scope. Moreover, the Application states, at page 12, lines 15-19, that "Weighted Tg averages for copolymers and polymers as set forth herein include from . . . about 0°C to about 40°C. Persons of ordinary skill in these arts, after reading this disclosure, will appreciate that all ranges and values within these explicitly stated ranges are contemplated." This disclosure provides **explicit** support for all ranges and values from about 0°C to about 40°C, **including the claimed range** starting at 26 °C, such that 35 U.S.C. §112¶1 is explicitly satisfied.

The Examiner is respectfully reminded that, going forward, the burden of proof lies with the Patent Office to establish a written description rejection. As stated at MPEP 2163.04, a description as filed is presumed to be adequate, unless or until **sufficient evidence or reasoning to the contrary** has been presented by the examiner to rebut the presumption. The Patent Office

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has the **initial burden of presenting by a preponderance of evidence** why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims.

Allowance of claims 167, 170-189, 206, and new claims 214-215 is requested.

II. Claims rejected in light of Alvarado and Tartaglia

Claims 54-75, 77, 84, 92-104, 151-163, 167-182, 186-202, and 206-209 were rejected under 35 U.S.C. §103(a) for obviousness in light of U.S. Patent No. 6,530,950 (Alvarado) in view of U.S. Pat. No. 5,637,113 (Tartaglia). Tartaglia was cited to provide the claimed thickness. Claims 98, 207, and 208 have been cancelled.

The rejection of claims 54-75, 77, 84, 92-104, 151-163, 167-169, 190-202, 206, and 209 is traversed on the grounds that the amended claims are directed to an uncrosslinked polymer that is not taught or suggested by the cited references.

Alvarado teaches using *crosslinked* compositions on a device. As taught at column 8, lines 1-17 of Alvarado, a variety of polymer compositions were prepared in the studies conducted in support of the Alvarado, each of which had a crosslinking agent, as shown in every Table and all the Examples. Alvarado explicitly teaches that there is **one alternative composition with no crosslinker**, see column 8, lines 1-17. In that sole embodiment, monomers are polymerized in a batch reactor in the absence of a crosslinker to form an intermediate product that is not used for a coating or device. Then the polymer is pelleted for feeding **along with the crosslinker** and crosslinked when used. The artisan reading Alvarado will understand that a crosslinker is intended for use in the Alvarado compositions.

A crosslinked polymer has structural and functional characteristics that make it distinct from an uncrosslinked polymer. Crosslinking forms links between polymer chains and affects a variety of physical properties, e.g., elasticity and strength. And, as discussed in the attached

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disclosure entitled "Glass transition temperature", crosslinked compositions generally do not have a glass transition temperature. Significantly, at the bottom of the Table 1, column 8, line 40, Alvarado explains that the glass transition temperatures for crosslinked compositions were calculated, not measured. In contrast, as taught in the Application, the claimed uncrosslinked structures having a glass transition temperature have advantages with respect to therapeutic agent delivery, e.g., at page 21, lines 21-23, wherein the Application states that a significant factor to control agent release is to achieve a particular average glass transition temperature for agent-release applications in (or on) a patient's body. Respectfully, it would be improper hindsight to apply the teaching of the Application to change the principle of operation of Alvarado to create the claimed coatings.

The rejection of claims 54-75, 77, 84, 92-104, 151-163, 167-169, 190-202, 206, and 209 is further traversed on the grounds that, contrary to the Office Action, Alvarado does not teach or suggest the claimed coating. Instead, Alvarado teaches making a stent entirely from certain polymers, or using those polymers to make a sleeve to fit over a stent. In the Field of the Invention, Alvarado states that the invention relates to (i) a stent for insertion into a body lumen and (ii) a stent having a **polymer sleeve** formed of the disclosed compositions. The sleeve embodiment is set forth in Figure 3B, which is described at columns 12, lines 28-40 and quoted with added emphases as follows:

> "FIG. 3B shows the metal stent of FIG. 3A with a continuous **polymer sheath** 30 encasing the metal support stent. The **outer polymer sleeve** is prepared, for example, as set forth in Example 1, and is composed of a polymer composition described above, especially with respect to the compositions set forth in Tables 1-6. The **sleeve** is carried coaxially about the outer circumference of the support stent and takes the form of a **flat sheet rolled into a cylindrical** or **tubular shape** by overlapping the edges 32, 34 of the

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sheet. It will be appreciated that the initial configuration of the tubular member is not limited to a flat sheet, but can also be prepared from an **extruded tube-form** or from a **molded tube-form.**"

Alvarado thus describes a **sheath, sleeve, extruded tube-**form and a **molded-tube** form. **Alvarado does not, however, describe the claimed coating.** The claimed coating is **not the same as, and is not comparable to,** the sleeve taught by Alvarado. For example, as explained in part in the Application at page 17, line 17 et seq., polymeric coatings are formed on an object. Forming the coating on the object gives rise to distinct physical properties at the material-to-device interface that are not present in a sleeve. A process of coating creates an intimacy of contact coating and the device that is often desirable. For instance, *paint* versus *siding* can both be options for covering an exterior surface of a dwelling. Paint forms a layer whereas siding is an overlay. The paint industry and the housing-siding industry provide different products with different advantages and disadvantages. Similarly, the claimed coating is distinct from the overlaying sleeve of Alvarado.

The other cited reference, Tartaglia, reinforces this same point because it is directed towards sleeves as opposed to the claimed coatings. Tartaglia teaches a film wrapped around a stent (column 1, line 45). A film wrapped around a stent is not the claimed coating and has distinct structural properties relative to a coating.

The rejection of amended claims 190-206 and 209 is further traversed on the grounds that the cited references do not teach or suggest the claimed devices.

III. Regarding 35 U.S.C. §103(a) rejections made with Lentz et al.

Claims 76, 78-83, 85, 91, 164-166, 183-185, and 203-205 were rejected under 35 U.S.C. §103(a) as being unpatentable over Alvarado et al. in view of Tartaglia and U.S. Pat. Pub. No. 2002/0133173 to Lentz et al. Lentz et al., however, does not make-up for the deficiencies of

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Alvarado et al. and Tartaglia that are discussed above. Moreover, Alvarado is directed to a sleeve that fits over a stent such that coating the sleeve of Alvarado with heparin of Tartaglia would not result in an operable invention since the heparin would be outside the stent and effectively not in contact with blood flowing through the lumen of the stent, thus defeating the point of adding a heparin layer. Allowance of these claims is therefore requested.

IV. Regarding 35 U.S.C. §103(a) rejections made with Sahatjian et al.

Claims 86-90 were rejected under 35 U.S.C. §103(a) in light of Alvarado in combination with Tartaglia and U.S. Pat. No. 5,843,089 to Sahatjian et al. Sahatjian et al., however, does not make-up for the deficiencies of Alvarado et al. and Tartaglia that are discussed above. Further, Sahatjian et al. is directed to a hydrogel lining on a stent lumen and not an exterior sleeve, as in Alvarado. Nor would there be a reasonable expectation of success when adding a hydrogel to the compositions of Alvarado since a hydrogel has radically different physical properties than Alvarado's compositions, which are believed to exclude hydrogels. Moreover, coating the exterior sleeve of Alvarado with the hydrogel of Sahatjian et al. would not result in an operable invention since the hydrogel lining would be outside the stent and effectively not in contact with blood flowing through the lumen of the stent, thus defeating the point of having the hydrogel liner as stated in Sahatjian et al.

V. Regarding new claims 210-213

It is respectfully submitted that Alvarado teaches a sleeve on an exterior portion of a stent and does not teach or suggest the claimed coating on both a lumen and an exterior of the stent (claims 211, 213). It is further submitted that Alvarado teaches a sleeve that indiscriminately covers the gaps in the mesh of the stent such that it does not teach or suggest the claimed coating is disposed essentially only on the solid portions of the stent (claims 210, 212). Nor do the other
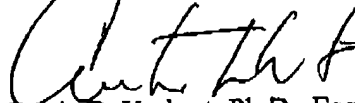
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cited references cure these deficiencies when considered in light of the other claimed features. Allowance of new claims 210-213 is accordingly requested.

Prayer for relief

In view of the foregoing, it is submitted that this application is in condition for allowance. Favorable consideration and prompt allowance of the application are respectfully requested.

The Examiner is invited to telephone the undersigned if the Examiner believes it would be useful to advance prosecution.

Respectfully submitted,

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Glass transition temperature

From Wikipedia, the free encyclopedia

A material's **glass transition temperature**, T_g, is the temperature below which molecules have little relative mobility. T_g is usually applicable to wholly or partially amorphous phases such as glasses and plastics. For inorganic or mineral glasses, such as common silicon dioxide (SiO_2) glass, it is the mid-point of a temperature range in which they gradually become more viscous and change from being liquid to solid. Thermoplastic (non-crosslinked) polymers are more complex because, in addition to a melting temperature, T_m, above which all their crystalline structure disappears, such plastics have a second, lower T_g below which they become rigid and brittle, and can crack and shatter under stress. Small molecular weight pure substances such as water have just one such condensed-phase temperature, below which they are solid crystals (or amorphous ice if cooled below T_g fast enough) and above which they are liquids.

Above T_g, the secondary, non-covalent bonds between the polymer chains become weak in comparison to thermal motion, and the polymer becomes rubbery and capable of elastic or plastic deformation without fracture. This behavior is one of the things which make most plastics useful. But such behavior is not exhibited by crosslinked thermosetting plastics which, once cured, are set for life and will shatter rather than deform, never becoming plastic again when heated, nor melting.

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Time dependency

Consider a molecular liquid which is slowly cooling down. At a certain temperature, the average kinetic energy of molecules no longer exceeds the binding energy between neighboring molecules and growth of organized solid crystal begins. Formation of an ordered system takes a certain amount of time since the molecules must move from their current location to energetically preferred points at crystal nodes. As temperature falls, molecular motion slows further down and, if the cooling rate is fast enough, molecules never reach their destination — the substance enters into dynamic arrest and a disordered, glassy solid (or supercooled liquid) forms. In fact, Kauzmann has argued that if such an arrest did not happen, at still lower temperatues a thermodynamically paradoxical situation would arise, where the undercooled liquid would have to be denser and of a lower enthalpy than the crystalline phase. Such arrest apparently takes place at certain temperature, which is called the *calorimetric ideal glass transition temperature* T_{0c}. This means that glass transition is not merely a kinetic effect, i.e. merely the result of fast cooling of a melt, but there is an underlying thermodynamic basis for glass formation. The glass transition temperature $T_g \to T_{0c}$ as $dT/dt \to 0$.

A full discussion of T_g requires an understanding of mechanical loss mechanisms (vibrational and resonance modes) of specific (usually common in a given material) functional groups and molecular arrangements. Factors such as heat treatment and molecular re-arrangement, vacancies, induced strain and other factors affecting the condition of a material may have an effect on T_g ranging from the subtle to the dramatic. T_g is dependent on the viscoelastic materials properties, and so varies with rate of applied load. The silicone toy 'Silly Putty' is a good

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example of this: pull slowly and it flows; hit it with a hammer and it shatters.

In contrast to the melting points of crystalline materials the glass transition temperature is therefore somewhat dependent on the time-scale of the imposed change. To some extent time and temperature are interchangeable quantities when dealing with glasses, a fact often expressed in the time-temperature superposition principle. An alternative way to discuss the same issue is to say that a glass transition temperature is only truly a point on the temperature scale if the change is imposed at one particular frequency. This is why the ability to modulate the temperature in a DSC experiment has made determining T_g considerably more precise. Since T_g is cooling-rate (or frequency) dependent as the glass is formed, the glass transition is not considered a true thermodynamic phase transition by many in the field. They reserve this epithet rather for a transition that is sharp and history-independent.

In polymers, T_g is often expressed as the temperature at which the Gibbs free energy is such that the activation energy for the cooperative movement of 50 or so elements of the polymer is exceeded. This allows molecular chains to slide past each other when a force is applied. From this definition, we can see that the introduction of relatively stiff chemical groups (such as benzene rings) will interfere with the flowing process and hence increase T_g. With thermoplastics, the stiffness of the material will drop due to this effect. This is shown in the figure below. It can be seen that when the glass temperature has been reached, the stiffness stays the same for a while, until the material melts. This region is called the rubber plateau.
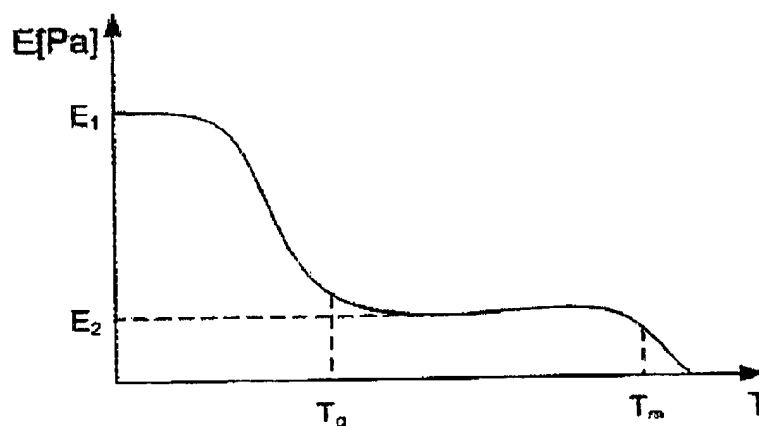
T_g can be significantly decreased by addition of plasticizers into the polymer matrix. Smaller molecules of plasticizer embed themselves between the polymer chains, increasing the spacing and free volume, and allowing them to move past one another even at lower temperatures. The "new-car smell" is due to the initial outgassing of volatile small-molecule plasticizers used to modify interior plastics (e.g., dashboards) to keep them from cracking in the cold, winter weather. The addition of nonreactive side groups to a polymer can also make the chains stand off from one another, reducing T_g. If a plastic with some desirable properties has a T_g which is too high, it can sometimes be combined with another in a copolymer or composite material with a T_g below the temperature of intended use. Note that some plastics are used at high temperatures, e.g., in automobile engines, and others at low temperatures.

In glasses (including amorphous metals and gels), T_g is related to the energy required to break and re-form covalent bonds in a somewhat less than perfect (may be regarded as an understatement) 3D lattice of covalent bonds. The T_g is therefore influenced by the chemistry of the glass. E.g., add B, Na, K or Ca to a silica glass, which have a valency less than 4 and they help break up the 3D lattice and reduce the T_g. Add P which has a valency of 5 and it helps re-establish the 3D lattice, increasing T_g.

The Space Shuttle Challenger disaster was caused by rubber O-rings that were below their glass transition

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temperature on an unusually cold Florida morning, and thus could not flex adequately to form proper seals between sections of the two solid-fuel rocket boosters.

Biophysics

Proteins also possess a glass transition temperature below which both anharmonic motions and long-range correlated motion within a single molecule are quenched. The origin of this transition is primarily due to "caging" by glassy water[1], but can also be modeled in the absence of explicit water molecules, suggesting that part of the transition is due to internal protein dynamics.[2]

Vitrification (glass formation below the melting point) can occur when starting with a liquid such as water, usually through very rapid cooling or the introduction of agents that suppress the formation of ice crystals. This is in contrast to ordinary freezing which results in ice crystal formation. Additives used in cryobiology or produced naturally by organisms living in polar regions are called cryoprotectants. Vitrification technology is being used to cryopreserve cells, tissues and organs for transplantation.

Glass transition temperature of some materials

Polymer	T_g (°C)
Polyethylene (LDPE)	−125 or −30 also cited
Polypropylene (atactic)	−20
Poly(vinyl acetate) (PVAc)	28
Polyethylene terephthalate (PET)	69
Poly(vinyl alcohol) (PVA)	85
Poly(vinyl chloride) (PVC)	81
Polystyrene	95
Polypropylene (isotactic)	100
Poly(methylmethacrylate) (atactic)	105
Chalcogenide AsGeSeTe	245
ZBLAN	265
Tellurite	279
Fluoroaluminate	400
Silica	1175

These are only mean values, as the glass transition temperature depends on the cooling-ratio, molecular weight distribution and could be influenced by additives.

Note also that for a semi-crystalline material such as Polyethylene that is 60-80% crystalline at room temperature the quoted glass transition refers to what happens to the amorphous part of the material as the temperature is dropped

See also

- Differential scanning calorimetry
- Vitrification

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2. ^ Salsbury FR, Han WG, Noodleman L, Brooks CL (2003). "Temperature-dependent behavior of protein-chromophore interactions: A theoretical study of a blue fluorescent antibody". *CHEMPHYSCHEM* 4: 848–855. Entrez PubMed 12961983 (http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12961983)

External links

- Vogel-Tammann-Fulcher Equation Parameters (http://www.ptbf.am.wroc.pl/v271/v271_17.pdf)
- Fragility thy name is glass (http://eprints.iisc.ernet.in/archive/00000257/01/kjrao.pdf)

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Categories: Biophysics | Condensed matter physics | Cryobiology | Polymer chemistry | Proteins

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